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Research Article

THE EFFECTS OF EXERCISE ON CENTRAL BLOOD VOLUME IN MAN

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It is well established that redistribution of the circulating blood volume occurs in a variety of conditions and following the exhibition of a number of pharmacologic agents. An augmentation of central blood volume has been demonstrated when an erect subject assumes the recumbent position (1–3), after the inflation of an antigravity suit (3, 4), following immersion of the body in water (4), after the administration of sympathomimetic amines (5–7), and when large volumes of blood are transfused to subjects under ganglionic blockade (8). A shift of blood out of the thorax occurs when the erect position is assumed (1, 2, 9), following the application of spinal and general anesthesia (10), positive pressure breathing (7, 11), the Flack maneuver (12), venous tourniquets to the extremities (3), and after the administration of ganglionic blocking agents (13, 14). Considerable difference of opinion exists, however, regarding the influence of muscular exercise on the central blood volume. Some observers (15, 16) have demonstrated a shift of blood out of the thorax; others have found either no consistent (17) or no significant (18) changes, while an increase in the central blood volume has been reported by Mankin and Swan (19) and by Mitchell, Sproule and Chapman (20, 21). Since a more complete understanding of the circulatory adaptations to exercise would be facilitated by clarification of this problem the present study was undertaken.

METHODS

The 10 subjects, all healthy males ranging in age from 18 to 24 years, were studied in the basal postabsorptive state following the oral administration of 75 or 100 mg of sodium pentobarbital. They had all been thoroughly familiarized beforehand with the laboratory, the equipment and the procedure. Simultaneous with each cardiac output and central blood volume measurement, the minute ventilation, oxygen consumption and respiratory quotient were determined by an open circuit respiratory system utilizing the micro-Scholander technic (22) for the analysis of expired air.

Cardiac output and central blood volume were measured with the indicator-dilution technic. Approximately 10 mg of Evans blue dye was injected from a tared syringe through a 50 cm polyethylene catheter (PE 50, 0.58 mm ID) which was introduced percutaneously through an antecubital vein into the superior vena cava or right atrium. Blood was sampled from the brachial artery through an indwelling arterial needle and was delivered to a cuvette densitometer (23) by means of a polyethylene catheter having a volume of 0.40 ml. The blood was withdrawn with a motor-driven suction syringe at a rate of 20 ml per minute. The volume of the cuvette is 0.30 ml and the response of the densitometer to a sudden change in density is 95 per cent in 1 second and over 99 per cent in 2 seconds (24). The arterial and central venous pressures were recorded by means of Statham pressure transducers immediately before and after each dilution curve. The electrocardiogram, pressure pulses, dilution curves, and the signal marking the instant of injection were inscribed with a photographic cathode-ray recorder at a paper speed of 5 mm per second.

Each dilution curve was calibrated separately in the following manner. Two arterial blood samples were collected in heparinized syringes immediately before the output determinations. These were delivered under oil into Erlenmeyer flasks, one of which contained approximately 0.5 mg of Evans blue dye. One of the two blood samples served as a blank. The second sample contained blood with a dye concentration of approximately 20 mg per L. After the dilution curve had been recorded, the blank sample and the sample containing dye were drawn in turn through the cuvette densitometer. The same flow rate and densitometer attenuation were employed as during the inscription of the original dilution curve. The alterations in the densitometer signal were recorded and related to the actual concentration of the sample, which was determined by subsequent spectrophotometric analysis. Only a two-sample calibration is required, since the output of the densitometer is linear with respect to dye concentration (23, 25).

The cardiac output and central blood volume were calculated utilizing the formulas of Stewart and Hamilton (26) after the inscribed dilution curves had been re-

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TABLE I

*Hemodynamic observations at rest and during exercise and recovery**

Subject BSA	Condition	$\dot{V}O_2$/M²	C.I.	A–VO_2	CBV	CBV/M²	SV_2/M²	Art. pressure	H.R.	SWLV/M²	TPR/M²	VENT/M²	R.Q.	ΔCO/$\Delta\dot{V}O_2$
C. B.	Rest	122	2.86	4.3	1,060	570	39.1	132/82 (104)	73	55.4	2,826	3.6	0.86	
1.86	Exercise	860	7.31	11.8	1,805	970	49.7	183/104 (129)	147	87.2	1,411	20.1	0.95	603
	Recovery	134	2.82	4.7	1,025	550	43.4	118/78 (95)	65	56.4	2,478	3.7	0.80	
E. F.	Rest	163	3.87	4.2	1,660	830	62.5	138/66 (81)	62	68.8	1,548	3.7	0.81	
2.00	Exercise	997	8.94	11.1	1,931	966	58.5	181/87 (117)	153	93.0	1,001	20.1	0.90	610
	Recovery	158	4.83	3.3	1,496	748	48.3	114/71 (87)	100	57.7	1,390	3.9	0.84	
B. K.	Rest	159	3.22	4.9	1,561	908	40.8	125/82 (97)	79	53.8	2,380	3.2	0.74	
1.72	Exercise	1,248	9.03	13.8	1,900	1,105	50.2	193/96 (127)	180	90.7	1,115	37.4	1.03	533
	Recovery	187	4.18	4.5	1,530	890	41.7	123/75 (92)	100	30.4	1,761	3.6	0.60	
R. S.	Rest	118	2.10	5.6	1,449	779	42.0	110/53 (70)	50	39.9	2,516	3.3	0.73	
1.86	Exercise	644	6.37	10.1	1,590	855	49.0	172/76 (112)	130	74.6	1,382	19.2	0.70	811
	Recovery	127	2.39	5.3	1,463	787	42.0	127/68 (82)	57	46.8	2,672	3.6	0.81	
J. L.	Rest	150	4.95	3.1	1,972	1,096	69.7	109/63 (83)	71	78.6	1,228	3.4	0.73	
1.80	Exercise	1,313	8.66	15.2	1,575	875	54.2	162/99 (109)	160	80.3	950	30.7	0.96	320
	Recovery	162	3.84	4.2	1,424	791	43.6	99/63 (75)	88	44.5	1,499	3.6	0.71	
D. B.	Rest	114	3.09	3.7	1,818	900	49.9	120/71 (90)	62	61.0	2,223	3.2	0.92	
2.02	Exercise	1,303	8.87	14.7	2,492	1,234	53.5	188/103 (136)	166	98.9	1,171	31.1	0.94	486
	Recovery	196	4.18	4.7	1,791	887	46.4	142/85 (107)	90	67.6	1,989	5.0	0.82	
J. H.	Rest	155	4.37	3.6	2,057	1,060	50.2	156/78 (106)	87	72.3	1,867	3.1	0.68	
1.94	Exercise	992	7.52	13.2	2,036	1,049	42.5	224/90 (132)	177	76.3	1,360	22.2	0.95	377
	Recovery	175	3.69	4.8	1,725	889	36.9	135/77 (91)	100	45.6	1,908	3.5	0.58	
J. R.†	Rest	150	2.93	5.1	1,139	575	34.0	100/62 (76)	86	35.2	2,047	3.1	0.67	
1.98	Exercise	884	6.76	13.1	1,629	822	49.0	144/73 (102)	138	68.0	1,206	16.0	0.90	523
	Recovery	188	3.63	5.2	1,399	707	42.6	116/78 (88)	91	47.7	1,917	5.3	0.88	
D. L.†	Rest	166	3.37	5.0	1,308	703	48.1	90/56 (70)	70	45.8	1,662	3.9	0.82	
1.85	Exercise	881	7.47	11.8	1,474	797	48.2	139/70 (98)	155	64.2	1,049	18.1	0.91	574
	Recovery	250	4.10	6.1	1,212	655	41.8	104/67 (82)	98	46.6	1,600	7.5	0.87	
J. P.†	Rest	143	3.46	4.2	1,763	979	54.9	110/71 (89)	63	66.4	2,012	3.2	0.74	
1.80	Exercise	983	8.95	11.0	2,203	1,224	49.7	170/98 (121)	180	81.8	1,062	25.1	1.01	655
	Recovery	177	4.91	3.6	1,825	1,014	54.6	100/71 (86)	90	63.3	1,385	3.6	0.60	

* BSA = body surface area in m².
C.I. = cardiac index in L per minute per m².
CBV = central blood volume in ml.
VENT/M² = ventilation in L per minute per m².
$\dot{V}O_2$/M² = oxygen consumption in ml per minute per m².
R.Q. = respiratory quotient.
A–VO_2 = arterio-mixed venous oxygen difference in vol per 100 ml.
H.R. = heart rate.
Art. press. = arterial pressure in mm Hg systolic/diastolic (mean).
SV/M² = stroke volume per m².
SWLV/M² = stroke work of left ventricle per m².
TPR/M² = calculated total peripheral vascular resistance per m².
† In subjects J. R., D. L., and J. F., data derived from dilution curves obtained from heated arm are listed.

plotted on semilogarithmic paper. The accuracy of the technics employed in the present investigation for the measurement of cardiac output and of central blood volume had previously been validated by direct measurements in circulatory models (7, 27) and in studies using flowmeters for the measurement of cardiac output in dogs (7, 25). The reproducibility of the cardiac output and central blood volume measurements by the technics used in this study was first determined by 23 duplicate determinations performed 10 minutes apart. The standard error of the duplicate determinations of central blood volume was 115 ml; that of the cardiac output was 493 ml per minute.

Fifteen to 20 minutes after the needles and catheter had been inserted, the control measurements were made with the subjects supine, but with their feet placed on the pedals of a bicycle ergometer. Exercise consisted of pedaling the ergometer at a constant rate of 50 to 60 rpm at an external work load of approximately 3,000 foot-pounds per minute for 10 minutes. Measurements were repeated during the last 2 minutes of the exercise period and again 20 minutes following the cessation of exercise, with the feet still in place on the bicycle.

In 3 of the 10 subjects the procedure was modified in order to minimize the possible effects on the calculated central blood volume of any vasoconstriction that might occur in the arm during leg exercise. Indwelling needles were placed in both brachial arteries and dilution curves were inscribed simultaneously from each artery. Hyperemia was induced in one arm by wrapping it completely in hot moist towels covered with electric heating pads. Dilution curves were then recorded from both arms during rest, exercise and recovery periods, as described above. The two simultaneously-determined cardiac outputs showed little difference. Their average was multiplied by the mean circulation times to both brachial arteries in the calculation of the central blood volumes between the site of injection and each sampling site.

Arteriovenous oxygen difference was calculated as the quotient of the oxygen consumption and the cardiac output; left ventricular stroke work index in gram-centimeters was calculated as the product of the stroke volume per square meter of body surface area and the mean arterial pressure; total peripheral vascular resistance index in dynes-sec-cm^{-5} was calculated according to the following formula:

$$\frac{\text{BSA} \times 1{,}332 \times (\text{mean brachial arterial pressure} - \text{mean central venous pressure mm Hg})}{\text{cardiac output (ml per sec)}}$$

RESULTS

During exercise the oxygen consumption increased from an average of 144 to an average of 1,011 ml per minute per m^2, while cardiac index rose from an average of 3.42 to 7.99 L per minute per m^2 (Tables I and II). The central blood volume increased by 141 to 745 ml in eight subjects; it remained essentially unchanged in one subject (J.H.) and declined 397 ml in the tenth (J.L.) (Figure 1). For the group as a whole the increase in central blood volume averaged 285 ml. The oxygen consumption, cardiac output, and systemic vascular resistance had not returned completely to the control levels at the end of the 20 minute recovery period in most of the subjects. During this time interval the central blood volume declined in all ten subjects by an average of 375 ml, with a fall which ranged from 127 to 782 ml (Figure 1).

TABLE II

*Mean values (M) and standard deviations (SD) for hemodynamic observations listed in Table I**

		Rest			Exercise			Recovery		
$\dot{V}O_2/M^2$	M		144.			1,011.			175.	
	SD		19.2			217.			34.7	
C.I.	M		3.42			7.99			3.86	
	SD		0.81			1.02			0.79	
A–VO_2	M		4.2			12.7			4.5	
	SD		0.25			1.69			0.26	
CBV	M		1,579			1,864.			1,489.	
	SD		340.			319.			251.	
CBV/M^2	M		840.			990.			792.	
	SD		185.			160.			135.	
SV/M^2	M		49.1			50.5			44.1	
	SD		11.0			4.2			4.75	
		S	D	M	S	D	M	S	D	M
Art. pressure	M	119	68	87	176	90	118	118	73	89
	SD	19.4	10.2	13.0	24.6	12.6	12.9	25.8	6.5	8.9
H.R.	M		70.			159.			88.	
	SD		11.6			17.4			15.1	
SWLV/M^2	M		57.7			81.5			50.7	
	SD		14.3			11.1			10.8	
TPR/M^2	M		2,031.			1,171.			1,860.	
	SD		479			166			437.	
VENT/M^2	M		3.37			24.00			4.33	
	SD		0.27			6.9			1.28	
R.Q.	M		0.77			0.93			0.75	
	SD		0.08			0.10			0.12	
Δ CO/Δ $\dot{V}O_2$	M					549				
	SD					44.				

* For abbreviations see Table I.

TABLE III

Data derived from dilution curves obtained from heated and unheated arms

Subject		Rest		Exercise		Recovery	
		Heated	Unheated	Heated	Unheated	Heated	Unheated
J. R.	C.O.*	5.79		13.39		7.18	
	Mct.	11.8	14.0	7.3	8.1	11.7	13.6
	CBV	1,139	1,351	1,629	1,806	1,399	1,627
D. L.	C.O.	6.23		13.82		7.58	
	Mct.	12.6	13.8	6.4	6.6	9.6	10.4
	CBV	1,308	1,432	1,474	1,520	1,212	1,314
J. P.	C.O.	6.22		16.12		8.83	
	Mct.	17.0	16.7	8.2	8.4	12.4	
	CBV	1,763	1,732	2,203	2,257	1,825	
Mean	Mct.	13.8	14.8	7.3	7.7	11.2	
	CBV	1,403	1,505	1,768	1,861	1,479	

* C.O. = cardiac output in L per minute; Mct. = mean circulation time in seconds; CBV = central blood volume in ml.

A comparison of the mean circulation times and central blood volumes derived from the curves obtained from the heated and unheated arms are presented in Table III. In three of the five comparisons carried out either at rest or during recovery, the value for the mean circulation times and calculated central blood volumes derived from the unheated arm exceeded the values obtained from the heated arm by 10 per cent or more. During exercise the difference exceeded 10 per cent in one subject (J.R.). Similar augmentations of the central blood volume during exercise and decreases during recovery were noted when the data calculated from the dilution curves recorded from the heated and unheated arms were compared. A representative pair of simultaneously inscribed dilution curves is illustrated in Figure 2.

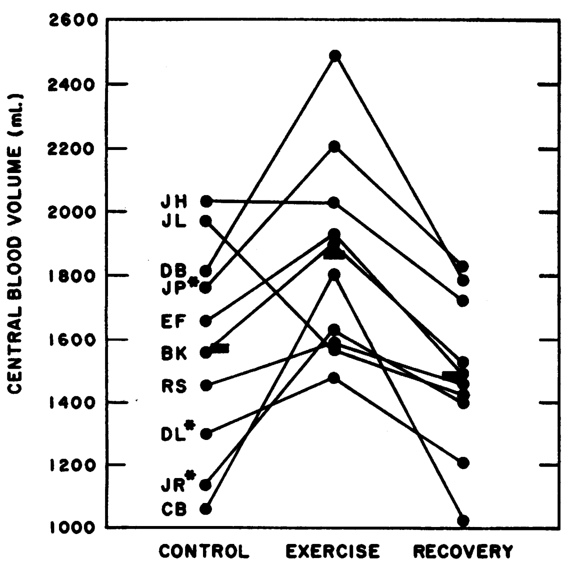

FIG. 1. CENTRAL BLOOD VOLUME MEASUREMENTS DURING CONTROL (REST), EXERCISE, AND RECOVERY PERIODS. Asterisks denote subjects in whom data were derived from dilution curves obtained by sampling blood from heated arm. Horizontal bars represent mean values for each period of observation.

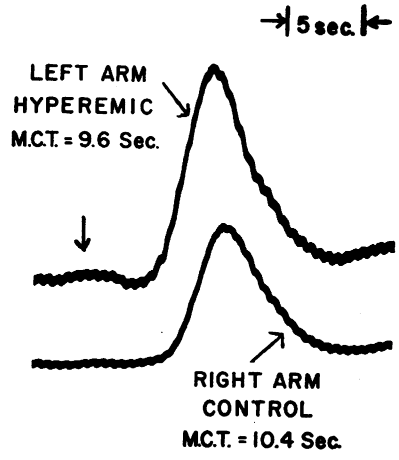

FIG. 2. DYE DILUTION CURVES INSCRIBED SIMULTANEOUSLY FROM HYPEREMIC LEFT ARM (UPPER CURVE) AND THE UNHEATED RIGHT ARM (LOWER CURVE) DURING THE RECOVERY PERIOD IN SUBJECT D.L. Vertical arrow indicates midpoint of injection corrected for the delay in the transit of blood from arterial needle to cuvette. M.C.T. refers to mean circulation time.

DISCUSSION

Consideration of the technics employed is pertinent to any comparison of the data obtained in the present study with previous investigations on the effect of exercise on central blood volume. Lammerant (16) utilized extrenal precordial counting technics in his investigation. Kattus, Mills, Klug and Pearce (15) employed the indicator-dilution technic, and determined central blood volume from the formula of Newman and associates (28). The validity of these methods for such determinations remains to be demonstrated. The applicability of the Stewart-Hamilton method to the accurate measurement of the volume of a segment of the vascular bed has been proved in experimental circulatory models (7, 27, 29) as well as in direct comparisons in the dog, both at normal (30) and elevated (31) pulmonary blood flows. Although other investigations (17, 19–21) on the effects of exercise on central blood volume have utilized the Stewart-Hamilton method, the volume measured was more nebulous than in the present study, since peripheral rather than central venous dye injections were made (32). The use of serial sampling technics in previous investigations (17, 20, 21) would also appear to be less desirable than the continuous recording of dye concentrations, particularly for the rapid dilution curves which characterize the exercise state.

The "central blood volume" determined in the present study is considered to represent the volume within the vascular bed between the site of injection in the right atrium or superior vena cava and the site of sampling in the brachial artery. It therefore comprises not only the blood in both sides of the heart and lungs, but also includes a significant fraction of the blood in the large arteries. It has recently been pointed out (33, 34) that the mean circulation time, and therefore the calculated central blood volume, may become falsely elevated when the rate of blood flow to the local site from which the dilution curve is sampled decreases. Thus, if the blood flow in the upper extremities decreased significantly during leg exercise, a spurious elevation of calculated central blood volume might result. Indeed, in the three subjects from whom dye curves were simultaneously recorded from both a hyperemic vasodilated arm and from the unheated opposite arm, slight differences in the mean circulation times, and therefore in the calculated central blood volumes, were apparent both at rest and during exercise (Table III). However, an increase in the calculated central blood volume during exercise and a decline during recovery occurred when the data obtained from both sampling sites were analyzed. Furthermore, it is pertinent that forearm blood flow does not decline in normal subjects during the eighth to tenth minutes (35, 36) of leg exercise. There is, therefore, little to suggest that the exercise-induced elevation in central blood volume described herein can be accounted for by alterations in blood flow to the site of sampling of the dilution curve.

Two of the subjects (J.L. and J.H.) did not demonstrate an augmentation in central blood volume during exercise as did the remainder of the group. Closer perusal of their hemodynamic data, however, may provide fuller insight into the cardiovascular adaptation to exercise. The resting indexes of cardiac output, of left ventricular stroke work, and of central blood volume in these two subjects were the highest values recorded for the entire group. Although the external work performed was identical in all subjects, J.L. and J.H. had the lowest absolute and relative increases in the left ventricular stroke work index, and in the cardiac output per unit increase in oxygen consumption; the cardiac outputs increased only 320 and 377 ml per minute, respectively, for each 100 ml increase in oxygen consumption. These two subjects were also the only two in the entire group who failed at least to double their resting cardiac outputs during exercise, and in whom both the cardiac output and central blood volume were distinctly lower during recovery from exercise than at rest. Clinical examination, however, failed to reveal any significant differences between J.L., J.H., and the rest of the group. It is not clear from the data at hand whether their inadequate elevation of cardiac output was due to failure of the central blood volume to rise or whether the reverse was the case. It appears, however, that the optimal cardiovascular response to exercise is characterized by an augmentation of central blood volume accompanying an elevation of cardiac output commensurate with the increased peripheral oxygen requirements.

Wade and co-workers (37) have demonstrated a shift of blood out of the splanchnic vascular bed during exercise. Wood and Bass (38) and Merritt and Weissler (39) have also indicated that venous tone in the upper extremities increases. It is certainly clear that the augmentation of the pulmonary diffusing capacity during exertion is accompanied by an elevation of the volume of blood within the capillary bed (40, 41). Thus, a number of investigations would be consonant with the view that a redistribution of circulating blood volume occurs during muscular exercise.

SUMMARY

The effect on central blood volume of ten minutes of moderately heavy leg exercise in the supine position was studied in ten normal subjects. Central blood volume was calculated by the Stewart-Hamilton formula from arterial dye-dilution curves following superior vena-caval or right atrial injection. During exercise the mean $\dot{V}O_2$ rose from 144 ± 19.2 to 1,011 ± 217 ml per m^2 and the cardiac index rose from a mean value of 3.42 ± 0.81 to 7.99 ± 1.02 L per minute per m^2. Central blood volume increased by 141 to 745 ml in eight subjects. For the entire group the increase in central blood volume averaged 285 ml. During 20 minutes of recovery the central blood volume declined in all ten subjects by an average of 375 ml, with a fall ranging from 127 to 782 ml.

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